Blood volume in angina pectoris

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SUMMARY Blood volume was measured in 60 consecutive male patients with disabling angina pectoris undergoing preoperative investigation for coronary bypass surgery. Of these patients, 58 had a lower blood volume than predicted. There was a decrease in blood volume of 21 per cent (1.3 litres) from the predicted normal value ($P < 0.001$). Seventeen per cent of the patients were on diuretics, 30 per cent were on digitalis, and 48 per cent were on beta-blocking drugs at the time of the study. There was no correlation between this medical treatment and the deviation in blood volume. In patients without signs of myocardial insufficiency the decrease in blood volume was most prominent, while in those with an enlarged heart and a raised left ventricular preload (at rest) the deviation was less.

Total blood volume is an important determinant of optimal cardiac function. Thus, increase in blood volume along with physical training is an adaptation and prerequisite for the increase in cardiac performance (Holmgren *et al.*, 1960). Several pathological conditions also influence the blood volume. Congestive heart failure is accompanied by an increase in total blood volume (Hedlund, 1953). Physical deconditioning resulting from long bed rest causes a decrease in the blood volume (Saltin *et al.*, 1968). Patients with valvular heart disease with no signs of heart failure, however, have a normal blood volume (Holmgren *et al.*, 1957). Patients with ischaemic heart disease are very sensitive to changes in magnitude and distribution of blood volume and particularly pulmonary blood volume. Shifting blood from the peripheral vascular bed to the lungs by changing from a sitting to a supine position will aggravate the symptoms of angina pectoris (Lecerof, 1971).

It is generally believed that the relief of angina by nitrates is caused by peripheral pooling accompanied by a decrease in ventricular volume (Mason and Braunwald, 1965; Williams *et al.*, 1965). In a study from this laboratory on the haemodynamic effects of beta-blockers in patients with angina pectoris it was found that total blood volume was low (Jonsson *et al.*, 1973; Åström *et al.*, 1976). The present investigation deals with a more elaborate study of blood volume in patients with angina pectoris accepted for preoperative investigation for bypass surgery.

Subjects and methods

Studies were made on 60 male patients with disabling angina pectoris. They were all assessed before operation for coronary bypass. Significant coronary artery disease was verified with selective angiography. The criteria for angina pectoris were typical chest pain elicited by effort and verified during an exercise test with a 6-lead chest electrocardiogram. Cardiac catheterisation was also performed in the majority of patients both at rest and during exercise.

Blood volume was calculated from the total amount of haemoglobin (THb), determined with the alveolar CO method of Sjöstrand (Sjöstrand, 1948; Holmgren, 1969) and haemoglobin concentration with correction to body haematocrit by a factor of 0.91. This method was used in 53 patients; in 7 patients the dilution method with radio-iodinated serum albumin (131 RIHSA) and a Volumetron was used (Williams and Fine, 1961). No significant difference was found between these two methods (A. Holmgren, 1976, unpublished observations). The age of the patients ranged between 34 and 64 years. Fifty per cent of the patients had had a previous myocardial infarction either from history or from the electrocardiogram. Fourteen patients (23%) had a normal resting electrocardiogram but all showed ST depression on exercise.

Thirty per cent of the patients were being treated with digitalis, 17 per cent with diuretics, and 48 per cent with beta-adrenergic blocking agents when referred to the clinic. In all patients the beta-blockade was stopped during the hospital stay and

in most of them also the other drugs. Forty-nine (82%) patients later went to bypass surgery.

Results

The normal value for THb in men in our laboratory is 10.46 ± 1.16 g/kg body weight and for blood volume 78.7 ± 5.9 ml/kg body weight (Holmgren, 1969). The blood volume in the patients with ischaemic heart disease averaged 4.74 ± 0.73 litres or 62.1 ± 7.8 ml/kg body weight. This is 1.3 litres less than predicted from the body weight. This difference of -21.1 per cent was highly significant ($P < 0.001$). In all patients except 2 the blood volume was lower than predicted (Fig. 1). The THb averaged 8.17 ± 1.17 g/kg body weight which is 21.9 per cent less than predicted ($P < 0.001$).

The patients with increased heart volumes tended to show smaller deviations from predicted blood volume (Fig. 2). All those with blood volumes below 25 per cent of predicted had normal heart volumes (< 500 ml/m² body surface area). Left ventricular filling pressure, measured as mean wedge pressure, was normal in most patients with angina pectoris at rest. However, those with wedge pressures above 15 mmHg had a smaller decrease in blood volume than the others (Fig. 3) and were within the normal range though still on the negative side. Of 60 patients, 46 were studied during heart catheterisation both at rest and exercise, and 41 (89%) of these had an abnormal increase in wedge pressure during exercise (Fig. 4).

Fig. 1 Blood volume in litres in patients with angina pectoris. Observed values (y axis) are given in relation to predicted (x axis) values. The 25 per cent reference line is shown.

Fig. 2 Heart volume (ml/m² body surface area) in relation to the relative decrease in blood volume from the predicted value (47/60 patients). Upper heart volume and lower blood volume normal limits are shown in straight lines.

Fig. 3 Pulmonary capillary wedge pressure in relation to the relative decrease in blood volume from the predicted value. Upper pulmonary capillary wedge pressure and lower blood volume normal limits are shown in straight lines.

Discussion

Blood volume in patients with disabling angina pectoris was found to average 79 per cent of that predicted. To our knowledge this has not been reported earlier. Gábor *et al.* (1976) have described a slight increase in blood volume in patients with ischaemic heart disease uncorrelated to angina pectoris.

The effect of medical treatment might have influenced our results. After long-term treatment

Fig. 4 Pulmonary capillary wedge pressure at rest (○) and during work (●) in relation to the cardiac output. Normal regression line is drawn.

with beta-blockade both a decrease in plasma volume (Tarazi *et al.*, 1971) and no change in plasma volume (Sederberg-Olsen and Ibsen, 1972; Hesse *et al.*, 1974) have been reported. However, we found no difference in blood volume between those who had been treated with beta-blockade and those who had not. Neither were there any differences between the groups on diuretics (17%) or digitalis (30%) and those without.

The majority of patients with angina pectoris were found to have normal end-diastolic left ventricular pressure at rest if not complicated by previous large myocardial infarction. However, during exercise when chest pain was precipitated the filling pressure of the left ventricle increased conspicuously, as a sign of acute reversible myocardial insufficiency.

Atrial receptors, when stimulated acutely, are known to cause increase in water and salt diuresis (Goetz *et al.*, 1975). However, Greenberg *et al.* (1973) have shown that in the presence of heart failure these receptors are depressed in their function. One might, therefore, expect an increase in blood volume in heart failure, or raised end-diastolic volume, and this correlates with our finding

that the blood volume reduction was less in the patients with heart failure.

Left ventricular receptors are stimulated by acute ventricular dilatation and such stimulation reduces renal sympathetic nervous activity and might, therefore, by renal vasodilatation lead to a diuresis (Öberg and White, 1970). In man, Bennett *et al.* (1977) have shown that there is an unexpected diuresis in the acute and early stage of left ventricular failure after myocardial infarction, but this does not persist. It might, therefore, be argued that in patients with angina who do not show a chronic rise in end-diastolic pressure or an enlarged heart, the constant short-lasting acute pressure rises associated with angina might lead to diuresis and hence to a reduction in blood volume (Sleight and Widdicombe, 1965).

Parker *et al.* (1970) have shown that acute phlebotomy relieved angina pectoris during pacing and normalised ventricular function. The homeostatic function of this reduction in blood volume would be to reduce the effect of the acute reversible myocardial insufficiency causing overdistension of the ventricle.

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